DICTIONARY FILE UPDATES: 28 MAR 2002 HIGHEST RN 403597-33-1

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

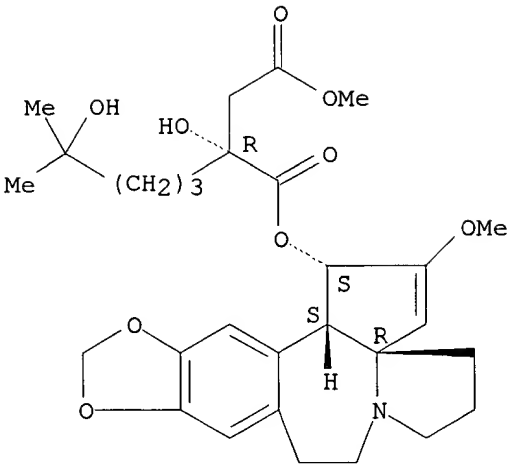
=> s homoharringtonine/cn
L1 1 HOMOHARRINGTONINE/CN

=> d l1

SM/2.11.10

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 26833-87-4 REGISTRY
CN Cephalotaxine, 4-methyl (2R)-2-hydroxy-2-(4-hydroxy-4-methylpentyl)butanedioate (ester) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Cyclopenta[a][1,3]dioxolo[4,5-h]pyrrolo[2,1-b][3]benzazepine, cephalotaxine deriv.
CN Cephalotaxine, 4-methyl 2-hydroxy-2-(4-hydroxy-4-methylpentyl)butanedioate (ester), [3(R)]-
CN **Homoharringtonine (8CI)**
OTHER NAMES:
CN NSC 141633
FS STEREOSEARCH
MF C29 H39 N O9
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NAPRALERT, PHAR, RTECS*, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

225 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
226 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.34	6.55

FILE 'CAPLUS' ENTERED AT 07:03:16 ON 01 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 1 Apr 2002 VOL 136 ISS 14
FILE LAST UPDATED: 28 Mar 2002 (20020328/ED)

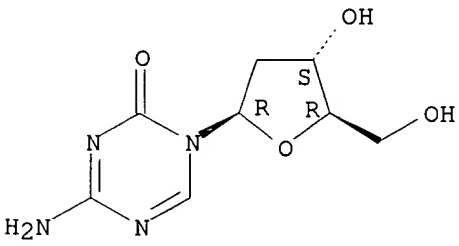
This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



43

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

356 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
357 REFERENCES IN FILE CAPLUS (1967 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s troxacytabine/cn
L3 0 TROXACYTABINE/CN

=> s cytosine arabinoside/cn
L4 1 CYTOSINE ARABINOSIDE/CN

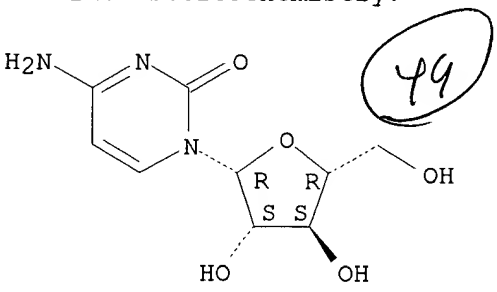
=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 147-94-4 REGISTRY
CN 2(1H)-Pyrimidinone, 4-amino-1-.beta.-D-arabinofuranosyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cytosine, 1-.beta.-D-arabinofuranosyl- (6CI, 8CI)
OTHER NAMES:
CN (Arabinofuranosyl)cytosine
CN 1-(.beta.-D-Arabinofuranosyl)cytosine
CN 1-(Arabinofuranosyl)cytosine
CN 1-.beta.-Arabinofuranosylcytosine
CN 1-.beta.-D-Arabinosylcytosine
CN 4-Amino-1-arabinofuranosyl-2-oxo-1,2-dihydropyrimidine
CN 58: PN: US6159940 SEQID: 71 claimed sequence
CN Ac 1075
CN Alexan
CN Ara-C
CN ara-Cytosine
CN Arabinocytosine
CN Arabinoside C
CN Aracytidine
CN Aracytin
CN Arafcyt
CN Citozar
CN Cyclocide
CN Cytarabin
CN Cytarabine
CN Cytarabinoside
CN Cytosar
CN Cytosine .beta.-D-arabinofuranoside
CN Cytosine .beta.-D-arabinoside
CN **Cytosine arabinoside**
CN Cytosine-1-.beta.-arabinofuranoside

514/211.09
514/211.10

CN Cytosine-1-.beta.-D-arabinofuranoside
CN DepoCyte
CN NSC 63878
CN Spongocytidine
CN U 19920
CN U 19920A
CN Udicil
FS STEREOSEARCH
MF C9 H13 N3 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



49

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4970 REFERENCES IN FILE CA (1967 TO DATE)
139 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4983 REFERENCES IN FILE CAPLUS (1967 TO DATE)
30 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.08	21.23

STN INTERNATIONAL LOGOFF AT 07:07:26 ON 08 FEB 2002

```
Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:sssptaul25jdg
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS  3  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS  4  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22  Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22  DGENE GETSIM has been improved
 NEWS  8  Oct 29  AAASD no longer available
 NEWS  9  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29  COPPERLIT now available on STN
 NEWS 12  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30  Files VETU and VETB to have open access
 NEWS 14  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10  DGENE BLAST Homology Search
 NEWS 16  Dec 17  WELDASEARCH now available on STN
 NEWS 17  Dec 17  STANDARDS now available on STN
 NEWS 18  Dec 17  New fields for DPCI
 NEWS 19  Dec 19  CAS Roles modified
 NEWS 20  Dec 19  1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25  Searching with the P indicator for Preparations
 NEWS 23  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:03:51 ON 08 FEB 2002

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

FILE 'REGISTRY' ENTERED AT 07:04:02 ON 08 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
```

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 6 FEB 2002 HIGHEST RN 390354-99-1
DICTIONARY FILE UPDATES: 6 FEB 2002 HIGHEST RN 390354-99-1

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved. Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies. Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

```
=> s azadeoxycytidine/cn
L1            0 AZADEOXYCYTIDINE/CN

=> s decitabine/cn
L2            1 DECITABINE/CN

=> d l2

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   2353-33-5  REGISTRY
CN   1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy-.beta.-D-erythro-
     pentofuranosyl)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   s-Triazin-2(1H)-one, 4-amino-1-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-
     (7CI, 8CI)
OTHER NAMES:
CN   2'-Deoxy-5-azacytidine
CN   2-Desoxy-5-azacytidine
CN   5-Aza-2'-deoxycytidine
CN   5-Azadeoxycytidine
CN   DAC
CN   Decitabine
CN   NSC 127716
FS   STEREOSEARCH
DR   123795-43-7, 105597-46-4
MF   C8 H12 N4 O4
CI   COM
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR,
       PROMT, RTECS*, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, WHO
```

```
Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:sssptau125jdg
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS  3  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS  4  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22  Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22  DGENE GETSIM has been improved
 NEWS  8  Oct 29  AAASD no longer available
 NEWS  9  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29  COPPERLIT now available on STN
 NEWS 12  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30  Files VETU and VETB to have open access
 NEWS 14  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10  DGENE BLAST Homology Search
 NEWS 16  Dec 17  WELDASEARCH now available on STN
 NEWS 17  Dec 17  STANDARDS now available on STN
 NEWS 18  Dec 17  New fields for DPCI
 NEWS 19  Dec 19  CAS Roles modified
 NEWS 20  Dec 19  1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25  Searching with the P indicator for Preparations
 NEWS 23  Jan 29  FSTA has been reloaded and moves to weekly updates

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *



FILE 'HOME' ENTERED AT 10:24:04 ON 31 JAN 2002

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

FILE 'REGISTRY' ENTERED AT 10:24:16 ON 31 JAN 2002
```

STRUCTURE FILE UPDATES: 30 JAN 2002 HIGHEST RN 388563-50-6
DICTIONARY FILE UPDATES: 30 JAN 2002 HIGHEST RN 388563-50-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved. Also, note that searches
conducted using the PREP role indicator were not affected.

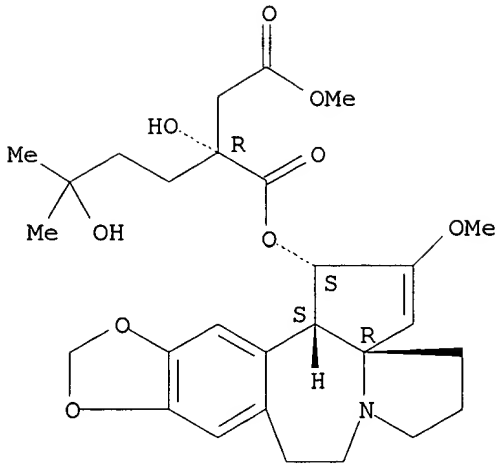
Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies. Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

```
=> s harringtonine/cn
L1            1 HARRINGTONINE/CN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   26833-85-2  REGISTRY
CN   Cephalotaxine, 4-methyl (2R)-2-hydroxy-2-(3-hydroxy-3-
     methylbutyl)butanedioate (ester) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4H-Cyclopenta[a][1,3]dioxolo[4,5-h]pyrrolo[2,1-b][3]benzazepine,
     cephalotaxine deriv.
CN   Cephalotaxine, 4-methyl 2-hydroxy-2-(3-hydroxy-3-methylbutyl)butanedioate
     (ester), [3(R)]-
CN   Harringtonine (8CI)
OTHER NAMES:
CN   2'R-Harringtonine
CN   Harringtonin
FS   STEREOSEARCH
DR   25302-09-4, 88455-80-5
MF   C28 H37 N O9
CI   COM
LC   STN Files:   ADISINSIGHT, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, DDFU,
       DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, NAPRALERT, PROMT, RTECS*,
       SPECINFO, TOXCENTER, TOXLIT, USPATFULL
         (*File contains numerically searchable property data)
```

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

212 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
212 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.22	6.37

FILE 'CAPLUS' ENTERED AT 10:25:21 ON 31 JAN 2002

FILE COVERS 1907 - 31 Jan 2002 VOL 136 ISS 5
FILE LAST UPDATED: 30 Jan 2002 (20020130/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> s l1 and cancer
214 L1

```
        153661 CANCER
         21100 CANCERS
        159896 CANCER
                  (CANCER OR CANCERS)
L2          15 L1 AND CANCER

=> d l2 1-15 all

L2   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2002 ACS
AN   2000:644675  CAPLUS
DN   134:36759
TI   Induction of apoptosis by harringtonine in HeLa cells
AU   Song, Changcheng; Xing, Luzhou; Song, Xiaoyuan; Peng, An; Wang, Yongchao
CS   Key Lab. Cell Proliferation Regulation Biology, Beijing Normal Univ.,
     Beijing, 100875, Peop. Rep. China
SO   Beijing Shifan Daxue Xuebao, Ziran Kexueban (2000), 36(3), 394-399
     CODEN: BSDKDH; ISSN: 0476-0301
PB   Beijing Shifan Daxue Xuebao Ziran Kexueban Bianjibu
DT   Journal
LA   Chinese
CC   1-6 (Pharmacology)
AB   The anticancer drug harringtonine (HT) which can induce apoptosis is
     investigated in HeLa cells by Hoechst 33342 nucleic staining, agarose gel
     electrophoresis of DNA and flow cytometry.  Typical apoptotic cell death
     is obsd. from 2 to 24 h and it increases in both dose- and time-dependent
     fashion.  The mechanism of HT-induced HeLa apoptosis is studied with
     synchronized cells and measuring gene expression.  The results demonstrate
     that the expression of bcl-2 decreases in G1 and G2 and keeps relatively
     stable in S phase, this agree with FCM results that HT induces HeLa cell
     apoptosis and S phase cells increasing.  In addn., HT induces down
     regulation of c-myc to inhibit cell proliferation and delays the
     progression of apoptosis.  These results are important to understand the
     mechanism of action of HT and to improve the effect of HT in
     cancer chemotherapy.
ST   apoptosis cell cycle harringtonine antitumor
IT   Proteins, specific or class
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (bcl-2; induction of apoptosis by harringtonine in HeLa cells)
IT   Gene, animal
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (c-myc; induction of apoptosis by harringtonine in HeLa cells)
IT   Antitumor agents
     Apoptosis
     Cell cycle
        (induction of apoptosis by harringtonine in HeLa cells)
IT   26833-85-2, Harringtonine
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (induction of apoptosis by harringtonine in HeLa cells)

L2   ANSWER 2 OF 15  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:581358  CAPLUS
DN   132:148682
TI   Establishment of multidrug-resistance leukemia cell line HL-60/H and its
     biological features
AU   Hong, Dengli; Zhang, Yaozhen; Zhang, Donghua; Shen, Guanxin; Shao,
     Jingfang; Li, Dengju; Cao, Wenjing; Liu, Wenli
CS   Department of Hematology, Tongji Hospital, Tongji Medical University,
     Wuhan, 430030, Peop. Rep. China
SO   Tongji Yike Daxue Xuebao (1999), 28(4), 302-305
     CODEN: TYDXEP; ISSN: 0258-2090
PB   Tongji Yike Daxue
DT   Journal
LA   Chinese
CC   9-11 (Biochemical Methods)
     Section cross-reference(s): 1
AB   A multidrug-resistance leukemia cell line HL-60/H resistant to
```

harringtonine (H) was cloned and screened by limit-dilg. method by gradually increasing dosage of H to study drug-resistance and drug-induced apoptosis. Biol. features of HL-60/H were measured by flow cytometry, transmission electron microscope, DNA fragmentation assay and immunohistochem. The results showed that HL-60/H cells had as 89.2-fold higher resistance to H compared to HL-60 cells. IC50 of H for HL-60/H did not markedly decrease after subculture 16 times in the medium without H. HL-60/H cells were cross-resistant to many other kinds of anti-**cancer** drugs. The expression of P-170 and BCL-2 obviously increased in HL-60/H cells. Intracellular daunorubicin accumulation in HL-60/H was much less than that in HL-60. It was not easy for H to induce apoptosis of HL-60/H cells. HL-60/H is a stable multidrug resistance cell sub-line. The important mechanism for HL-60/H cells resistant to drugs might be that drugs do not easily accumulate in cells because of the over-expression of P-170. HL-60/H cells are resistant to apoptosis induced by drugs because of the over-expression of BCL-2.

ST multi drug resistance leukemia cell line HL60 H apoptosis

IT Animal cell line
(HL-60/H; establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

IT P-glycoproteins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(P-170; establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(bcl-2; establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

IT Apoptosis
Leukemia
Multidrug resistance
(establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

IT 20830-81-3, Daunorubicin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(intracellular accumulation; establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

IT **26833-85-2**, Harringtonine
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(resistance; establishment of a multidrug-resistance leukemia cell line HL-60/H and its biol. features)

L2 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1998:316120 CAPLUS
DN 129:49320
TI Antisense expression of protein kinase C.alpha. improved sensitivity to anticancer drugs in human lung **cancer** LETPa-2 cells
AU Wang, Xiang-Yang; Liu, Hui-Tu
CS Dep. Biology, Beijing Normal Univ., Beijing, 100875, Peop. Rep. China
SO Zhongguo Yaoli Xuebao (1998), 19(3), 265-268
CODEN: CYLPDN; ISSN: 0253-9756
PB Kexue Chubanshe
DT Journal
LA English
CC 1-6 (Pharmacology)
AB AIM: to study the role of protein kinase C.alpha. (PKC.alpha.) in sensitivity to some clin. anticancer drugs in human lung **cancer** LTEPa-2 cells. METHODS: human lung **cancer** cell model expressing antisense PKC.alpha. was established and characterized by gene transfection and immunoblotting. Northern blotting was used to analyze the expression of multiple drug resistance (mdr-1) gene and antisense PKC.alpha. mRNA. IC50 for some anticancer drugs in cultured cells were measured. RESULTS: expression of antisense PKC.alpha. mRNA inhibited mdr-1 gene expression in lung **cancer** cells and improved

sensitivity to anticancer drugs (harringtonine, carboplatin, bleomycin A5, vincristine and doxorubicin) in lung **cancer** cells. IC50 for harringtonine, carboplatin, bleomycin A5, vincristine, and doxorubicin was decreased by 46.4 %, 42.1 %, 79 %, 69.9 %, and 61.6 % resp. CONCLUSION: PKC.alpha. plays an important regulation role of mdr-1 gene expression and drug sensitivity in human lung **cancer** cells.

ST lung **cancer** drug sensitivity protein kinase

IT Lung tumor inhibitors
(antisense expression of protein kinase C.alpha. improved sensitivity to anticancer drugs in human lung **cancer** LETPa-2 cells)

IT MDR1 gene (animal)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antisense expression of protein kinase C.alpha. improved sensitivity to anticancer drugs in human lung **cancer** LETPa-2 cells)

IT 57-22-7, Vincristine 11116-32-8, Bleomycin A5 23214-92-8, Doxorubicin **26833-85-2**, Harringtonine 41575-94-4, Carboplatin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense expression of protein kinase C.alpha. improved sensitivity to anticancer drugs in human lung **cancer** LETPa-2 cells)

IT 141436-78-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.; antisense expression of protein kinase C.alpha. improved sensitivity to anticancer drugs in human lung **cancer** LETPa-2 cells)

L2 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1996:305866 CAPLUS

DN 125:25740

TI A study on the mutagenicity of antineoplastic drugs and antimutagens against

AU Zhao, Z. Z.; Wen, D. G.; Wei, L. Z.; Zhu, H. M.; Zhao, W. Y.; Chen, C. Y.; Zhao, Y. L.; Gao, Y. Z.; Gu, S. K.

CS Hebei Cancer Institute, Shijiazhuang, Peop. Rep. China

SO Proc. Int. Cancer Congr., Free Pap. Posters, 16th (1994), Volume 1, 353-356. Editor(s): Rao, R. S. Publisher: Monduzzi Editore, Bologna, Italy.
CODEN: 62UYAO

DT Conference

LA English

CC 1-6 (Pharmacology)

AB With the aim to investigate the mutagenicity of antineoplastic drugs and to look for antimutagens against them, we examd. the mutagenicity of 22 commonly used antineoplastic agents by Ames test, SOS inductest, and SOS chromtest. We also examd. the possible action of 60 chinese herbs, fruits, vegetables and vitamins by SOS mutational and antimutational test. The result both with and without S9(rat liver microsomal enzymes) indicated that 17 (77.3%) of the 22 antineoplastic agents could induce mutagenesis in the testing strains; 36 types of natural plants, vitamins, and drinks could inhibit the mutagenicity of the antineoplastic agents. As the incidence of **cancer** continues to rise and the medicinal industry expands, there is a greet increase in the types and amt. of antineoplastic drugs produced. Many antineoplastic drugs are genetically toxic; recently attention has been paid to the mutagenicity of the drugs and to natural antimutagens against it.

ST antineoplastic drug mutagenicity antimutagen

IT Mutagens
Neoplasm inhibitors
(antineoplastic drug mutagenicity and antimutagens)

IT Pharmaceutical natural products
Vitamins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antineoplastic drug mutagenicity and antimutagens)

IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D 51-21-8, 5-Fluorouracil 51-75-2, Mustine 59-05-2, Methotrexate 125-84-8, Aminoglutethimide 147-94-4, Cytarabine 154-93-8, Carmustin

671-16-9, Procarbazine 865-21-4, Vinblastin 11056-06-7, Bleomycin 13010-47-4, Lomustine 13455-05-5, Thiophosphoramide 15663-27-1, Cisplatin 17902-23-7, Ftorafur 25316-40-9, Adriamycin **26833-85-2**, Harringtonin 33419-42-0, Etoposide 41575-94-4, Carboplatin 56390-09-1, Farmorubicin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(antineoplastic drug mutagenicity and antimutagens)

L2 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1995:678592 CAPLUS
DN 123:74386
TI Preliminary study of the effect of selected Chinese natural drugs on human ovarian **cancer** cells
AU Yu, Jing Jie; Reed, Eddie
CS National Cancer Institute, National Institutes Health, Bethesda, MD, 20892, USA
SO Oncol. Rep. (1995), 2(4), 571-5
CODEN: OCRPEW
DT Journal
LA English
CC 1-6 (Pharmacology)
AB This study investigated the in vitro anticancer effects of four Chinese natural drugs on the human ovarian **cancer** cell lines A2780 (cisplatin-sensitive) and A2780/CP70 (cisplatin-resistant). Cells were treated with series of concns. of drug prepns. for 24 h. Vincristine prepd. by the same pharmaceutical firm in China, was used as an internal control. As assessed by colony formation assays, harringtonine induced similar growth inhibiting effects in A2780 and A2780/CP70 cell lines with a 50% ID (IC50) of 0.195 .mu.g/mL in both. Rabdosia rubescens Hara demonstrated a cytotoxic effect on cisplatin-sensitive A2780 cells with an IC50 of 0.58 mg/mL; but there was no effect on A2780/CP70 cells. The data suggest direct antiproliferative activity for at least two Chinese natural medicines used in the clin. treatment of **cancer** in China. Further investigation of Chinese natural medicines may be valuable in the identification of new and effective anticancer drugs with minimal side effects.
ST Chinese natural drug ovary **cancer** resistance; cisplatin ovary **cancer** resistance Rabdosia antitumor; harringtonine juglone solanine norcantharidin ovary **cancer**
IT Drug resistance
Rabdosia rubescens
(Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)
IT Pharmaceutical natural products
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Chinese; Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)
IT Ovary, neoplasm
(inhibitors, Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)
IT Neoplasm inhibitors
(ovary, Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)
IT 15663-27-1, Cisplatin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)
IT 481-39-0, Juglone **26833-85-2**, Harringtonine 29745-04-8, Norcantharidin 51938-42-2, Solanine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Chinese natural drugs effects on human cisplatin-resistant ovarian **cancer** cells)

L2 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1995:290684 CAPLUS
DN 122:45924

TI Effect of harringtonine on apoptotic cell death and cell cycle progression in human leukemia HL60 cells
AU Liu, Yun-Peng; Ueda, Takanori; Yoshida, Akira; Iwasaki, Hiromichi; Nakamura, Toru
CS 1st Department Internal Medicine, Fukui Medical School, Fukui, 910-11, Japan
SO Anticancer Res. (1994), 14(4A), 1509-15
CODEN: ANTRD4; ISSN: 0250-7005
DT Journal
LA English
CC 1-6 (Pharmacology)
AB The mechanism of cell killing induced by harringtonine (HT) was investigated in HL60 cells by metabolic labeling studies, light and transmission electron microscopy, agarose gel electrophoresis of DNA, and flow cytometry. At concns. higher than 0.02 .mu.M HT showed significant inhibition on cell growth and protein and DNA synthesis. Following exposure to HT, typical apoptotic cell death was obsd. from 1.5 to 4 h and it increased in both dose-and time-dependent fashion. In addn., at 0.04 .mu.M of HT the nonapoptotic cells delayed the progression of cell cycle through S and G2 phase and finally arrested in G1 phase. These results are important to understand the mechanism of action of HT and to improve the effect of HT in **cancer** chemotherapy.
ST antitumor harringtonine apoptosis cell cycle
IT Apoptosis
Cell cycle
(harringtonine induction of apoptosis and effect on cell cycle progression in human leukemia cells in relation to antitumor effect)
IT Neoplasm inhibitors
(leukemia, harringtonine induction of apoptosis and effect on cell cycle progression in human leukemia cells in relation to antitumor effect)
IT **26833-85-2**, Harringtonine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(harringtonine induction of apoptosis and effect on cell cycle progression in human leukemia cells in relation to antitumor effect)

L2 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1993:462320 CAPLUS
DN 119:62320
TI Chemosensitivity testing of adenosystic, tongue and gigiva **cancer** cell lines
AU Wu, Junzheng; Situ, Zhenqiang; Chen, Jianyuan; Liu, Bin; Wang, Wei
CS Coll. Stomatol., 4th Mil. Med. Univ., Xian, 710032, Peop. Rep. China
SO Zhonghua Kouqiang Yixue Zazhi (1992), 27(2), 107-8
CODEN: ZKYZE2
DT Journal
LA Chinese
CC 1-1 (Pharmacology)
AB The in vitro MTT assay was used for examg. the chemosensitivity of human adenocarcinoma SACC-83, tongue **cancer** Tca 8113 and gingiva **cancer** Ca 9-22 cells to 14 antitumor agents. Adriamycin, methotrexate and 5-fluorouracil showed the highest activity against these cell lines. Cantharidin did not show any activity in this study.
ST antitumor chemosensitivity MTT assay cell line
IT Neoplasm inhibitors
(adenocarcinoma, chemosensitivity to, MTT assay for, in human cells)
IT Gingiva
(neoplasm, chemosensitivity of, to antitumor agents, MTT assay for, in human cells)
IT Tongue
(neoplasm, carcinoma, inhibitors, chemosensitivity of, MTT assay for, in human cells)
IT Neoplasm inhibitors
(tongue carcinoma, chemosensitivity of, MTT assay for, in human cells)
IT 298-93-1, MTT
RL: ANST (Analytical study)

(chemosensitivity assay using, in human adenocarcinoma and tongue **cancer** and gingiva **cancer** cells)

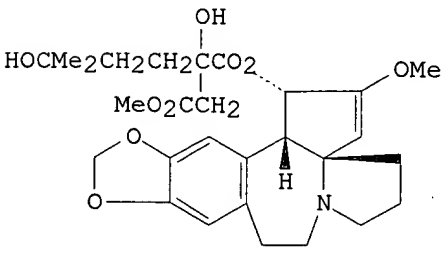
IT 50-07-7, Mitomycin C 50-76-0, Actinomycin D 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 55-86-7, Nitrogen mustard 56-25-7, Cantharidin 57-22-7, Vincristine 59-05-2, Methotrexate 66-97-7, Psoralen 147-94-4, Ara-C 15663-27-1, Cisplatin 23214-92-8, Adriamycin **26833-85-2**, Harringtonine 115038-62-5, Pingyangmycin
RL: ANST (Analytical study)
(tumor sensitivity to, MTT assay for, in human adenocarcinoma and tongue **cancer** and gingiva **cancer** cells)

L2 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1993:462310 CAPLUS
DN 119:62310
TI MTT assay and its application in chemosensitivity testing of antitumor Chinese medicine
AU Wu, Junzheng; Situ, Zhenqiang; Liu, Bin; Wang, Wei; Chen, Jianyuan
CS Coll. Stomatol., 4th Mil. Med. Univ., Chengdu, 710032, Peop. Rep. China
SO Zhonghua Kouqiang Yixue Zazhi (1992), 27(6), 373-5
CODEN: ZKYZE2
DT Journal
LA Chinese
CC 1-1 (Pharmacology)
AB A MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) colorimetric assay was used to examine the responses of human mucoepithelial **cancer** (MEC-1), adenosarcoma (SACC-83), tongue **cancer** (Tca 8113) and gingival **cancer** (Ca 9-22) cell lines to several antitumor Chinese medicines (psoralen, harringtonine, vincristine and cantharidin); the relative chemosensitivity of cells to pingyangmycin, mitomycin C or cisplatin was also tested. Results suggest that psoralen, harringtonine and vincristine have therapeutic potential for the treatment of **cancer** of the oral cavity and salivary gland.
ST antitumor chemosensitivity MTT oral cavity **cancer**
IT Neoplasm inhibitors
(salivary gland, testing of, in human cells, MTT chemosensitivity test for)
IT Neoplasm inhibitors
(mouth, testing of, in human cells, MTT chemosensitivity test for)
IT Salivary gland
(neoplasm, inhibitors, MTT chemosensitivity test for, in human cells)
IT Mouth
(neoplasm, inhibitors, testing of, in human cells, MTT chemosensitivity test for)
IT 50-07-7 56-25-7 57-22-7 66-97-7, Psoralen 15663-27-1 **26833-85-2** 115038-62-5, Pingyangmycin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, in human oral cavity and salivary gland **cancer** cells, MTT chemosensitivity test for)
IT 298-93-1, MTT
RL: ANST (Analytical study)
(**cancer** chemosensitivity test using, in human oral cavity and salivary gland **cancer** cells)

L2 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1989:50894 CAPLUS
DN 110:50894
TI Antagonistic interactions of hexamethylene bisacetamide in combination with 1-.beta.-D-arabinofuranosylcytosine, adriamycin and harringtonine on the growth and differentiation of HL-60 cells in vitro
AU Kong, Xiangbin; Fanucchi, Michael P.; Chou, Ting-Chao
CS Lab. Pharmacol., Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SO Leuk. Res. (1988), 12(10), 853-9
CODEN: LEREDD; ISSN: 0145-2126
DT Journal

LA English
CC 1-6 (Pharmacology)
AB Selective killing of **cancer** cells by cytotoxic agents and the conversion of cancerous cells to normal state by differentiation agents represent two basically different approaches in chemotherapy. The combinations of the cell differentiation-inducer hexamethylene bisacetamide (HMBA) and the cytotoxic agents 1-.beta.-D-arabinofuranosylcytosine (Ara-C), adriamycin (Adr), and harringtonine (HT) were examd. for cytotoxicity and induction of cell differentiation in HL-60 cells by measuring cell growth inhibition, morphol. maturation, and nitroblue tetrazolium (NBT) redn. After 5-day exposure to each drug alone the ED50s for cell growth inhibition were 0.01 .mu.M for Ara-C, 0.012 .mu.M for Adr, 0.017 .mu.M for HT, and 2.53 mM for HMBA. ED50s for differentiation were 0.089 .mu.M (morphol.) and 0.06 .mu.M (NBT) for Ara-C, 0.12 .mu.M (morphol.) and 0.09 .mu.M (NBT) for Adr, 0.04 .mu.M (morphol.) and 0.06 .mu.M (NBT) for HT, and 2.55 mM (morphol.) and 2.43 mM (NBT) for HMBA. at dose levels from ED50 to ED95, the combinations of Adr/HMBA and HT/HMBA had antagonistic cytotoxic and cell differentiation effects. The combination of Ara-C/HMBA had antagonistic cytotoxic effects but only slight synergistic cell differentiation effects. Thus, equipotency combinations of the above three pairs of drugs do not synergistically enhance cytotoxicity or cell differentiation effects in vitro to levels high enough for successful treatment of acute leukemia.
ST hexamethylene bisacetamide interaction antitumor leukemia differentiation; antitumor cytotoxicity differentiation leukemia drug interaction
IT Drug interactions
(of hexamethylene bisacetamide with antitumor agents, leukemic cell cytotoxicity or differentiation response to)
IT Toxicity
(cyto-, of antitumor drugs, hexamethylene bisacetamide interaction effects on leukemic cell)
IT Neoplasm inhibitors
(leukemia, adriamycin and arabinofuranosylcytosine and harringtonine, hexamethylene bisacetamide interaction with, leukemic cell cytotoxicity or differentiation response to)
IT 147-94-4, 1-.beta.-D-Arabinofuranosylcytosine 23214-92-8, Adriamycin **26833-85-2**, Harringtonine
RL: BIOL (Biological study)
(hexamethylene bisacetamide interaction with, leukemic cell cytotoxicity or differentiation response to)

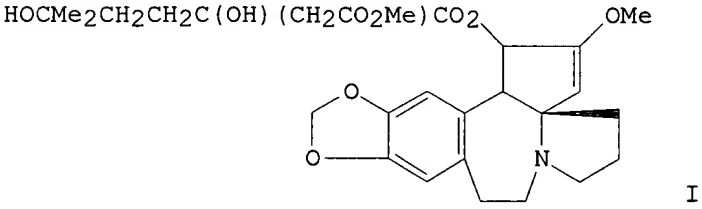
L2 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1983:463951 CAPLUS
DN 99:63951
TI Comparative in vitro antitumor activity of homoharringtonine and harringtonine against clonogenic human tumor cells
AU Jiang, T. L.; Liu, R. H.; Salmon, S. E.
CS Cancer Cent., Univ. Arizona, Tucson, AZ, 85724, USA
SO Invest. New Drugs (1983), 1(1), 21-5
CODEN: INNDDK
DT Journal
LA English
CC 1-6 (Pharmacology)
GI



I

DN 98:65182
TI Biochemical actions of some anticancer agents
AU Wu, Guoli; Nie, Jianchu; Yang, Huijun; Chen, Xing; Wei, Qun; Xiang, Huaming; Zhang, Yinghua
CS Dep. Biol., Beijing Normal Univ., Beijing, Peop. Rep. China
SO Beijing Shifan Daxue Xuebao, Ziran Kexueban (1982), (2), 57-66
CODEN: BSDKDH
DT Journal
LA Chinese
CC 1-6 (Pharmacology)
AB The effects of harringtonine [**26833-85-2**], cantharidate [54382-54-6], Zhu-ling (Polyporus unbellatus ext.), and Sarcandra glabra ext. on hepatoma H22, L-1210 leukemia, and tumor-bearing mice were studied. In hepatoma H22 cells, cantharidate and Zhu-ling ext. not only increased the intracellular levels of cAMP [60-92-4] and the cAMP/cGMP [7665-99-8] ratio, but also inhibited cAMP phosphodiesterase [9036-21-9] activity; in addn., cantharidate increased the cytoplasmic cAMP-dependent protein kinase [9026-43-1] activity. Harringtonine had similar effects on cyclic nucleotide metab. in L-1210 leukemia cells. Cantharidate, S. glabra ext., and Zhu-ling ext. affected the activities of 4 lysosomal enzymes, acid phosphatase [9001-77-8], DNase [9003-98-9], RNase [9001-99-4], and cathepsin D [9025-26-7]. Zhu-ling ext. restored the liver levels of glycogen [9005-79-2], glucose-6-phosphate [56-73-5], and fructose-1,6-diphosphate [488-69-7] in hepatoma H22-bearing mice. Cantharidate, Sarcandra glabra ext., and Zhu-ling ext. decreased O consumption in hepatoma H22 cells. In vitro, the respiration control index of hepatoma H22 cells was increased by these drugs. They also increased the liver succinic dehydrogenase [9002-02-2] and catalase [9001-05-2] in **cancer**-bearing mice.
ST anticancer drug enzyme; harringtonine enzyme metab neoplasia; cantharidate enzyme metab neoplasia; Zhu ling enzyme metab neoplasia
IT Neoplasm inhibitors
(animal metab. response to, in neoplasia)
IT Neoplasm, metabolism
(cantharidate and harringtonine and oriental plant exts. effect on)
IT Lysosome
(enzymes of liver, neoplasm inhibitors effect on, in neoplasia)
IT Polyporus umbellatus
Sarcandra glabra
(ext., animal metab. response to, in neoplasia)
IT Animal metabolism
Animal respiration
(in neoplasia, neoplasm inhibitors effect on)
IT Liver, metabolism
(neoplasm inhibitors effect on)
IT Nucleotides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cyclic, metab. of, neoplasm inhibitors effect on, in neoplasia)
IT 9026-43-1
RL: BIOL (Biological study)
(cAMP-dependent, of neoplasm, drugs effect on)
IT 60-92-4 7665-99-8
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, in neoplasm, drugs effect on)
IT **26833-85-2** 54382-54-6
RL: BIOL (Biological study)
(neoplasm metab. response to)
IT 9001-77-8 9001-99-4 9003-98-9 9025-26-7
RL: BIOL (Biological study)
(of liver lysosomes, neoplasm inhibitors effect on, in neoplasia)
IT 56-73-5 488-69-7 9001-05-2 9002-02-2 9005-79-2, biological studies
RL: BIOL (Biological study)
(of liver, neoplasm inhibitors effect on, in neoplasia)
IT 9036-21-9
RL: BIOL (Biological study)
(of neoplasm, drugs effect on)

L2 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1981:96250 CAPLUS
DN 94:96250
TI Mechanisms of action of harringtonine, a new anticancer agent
AU Zhenkun, Pan; Yongchao, Wang; Kun, Lee; Chingyi, Sze; Xiujuan, Ji; Yuting, Xu; Yijun, Fan; Zhanrong, Li; Rui, Han
CS Inst. Materia Med., Chin. Acad. Med. Sci., Beijing, Peop. Rep. China
SO Proc. - U.S.-China Pharmacol. Symp. (1980), Meeting Date 1979, 69-92. Editor(s): Burns, John J.; Tsuchitani, Patricia Jones. Publisher: NAS, Washington, D. C.
CODEN: 44XHAE
DT Conference
LA English
CC 1-6 (Pharmacodynamics)
GI



I

AB Harringtonine (I) [**26833-85-2**] (0.86-2 mg/kg, i.p., for 5-12 consecutive days) was effective against L-615 and L-1210 leukemias, sarcoma 180, Walker carcinosarcoma 256, and Lewis lung **cancer**. I was most active against leukemia and was found to be effective against myelocytic, acute monocytic, erythro- and other leukemias in humans. The mechanism of the antileukemic action of I is discussed.
ST antitumor harringtonine; leukemia inhibition harringtonine
IT Neoplasm inhibitors
(harringtonine, mechanism of action of)
IT **26833-85-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, mechanism of)

L2 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1974:445352 CAPLUS
DN 81:45352
TI Potentially useful combinations of chemotherapy detected in mouse tumor systems
AU Kline, Ira
CS Microbiol. Assoc., Inc., Bethesda, Md., USA
SO Cancer Chemother. Rep., Part 2 (1974), 4(1), 33-43
CODEN: CCSUBJ
DT Journal
LA English
CC 1-5 (Pharmacodynamics)
AB Combinations of ICRF-159 (I) [21416-87-5] with adriamycin [23214-92-8], daunorubicin [20830-81-3], camptothecin [7689-03-4], NSC 113089 [42013-69-4], cis-diamminedichloroplatinum [15663-27-1], and cytosine arabinoside [147-94-4] caused greater increases in the life-span of L1210 leukemia-bearing mice than did single-drug therapy. Other effective antileukemia drug combinations included NSC 45388 [4342-03-4] plus adriamycin, NSC 51143 [251-80-9], and camptothecin; camptothecin plus cyclophosphamide [50-18-0], isophosphamide [3778-73-2], and methotrexate [59-05-2]; 5-azacytidine [320-67-2] plus emetine [483-18-1]; and cytosine arabinoside plus NSC 82196 [5034-77-5].
ST neoplasm inhibitor combination therapy; leukemia therapy drug combination; **cancer** therapy drug combination
IT Leukemia
(inhibitors of, drug combinations as)

IT Neoplasm inhibitors
(leukemia treatment with, drug combinations in relation to)
IT 50-18-0 59-05-2 69-74-9 251-80-9 316-42-7 320-67-2 519-23-3
3778-73-2 4342-03-4 5034-77-5 6872-73-7 7059-24-7 10212-28-9
15663-27-1 19494-89-4 21416-87-5 23214-92-8 23541-50-6
25387-67-1 25662-95-7 **26833-85-2** 42013-69-4
RL: BIOL (Biological study)
(leukemia treatment with, drug combinations in relation to)

L2 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1972:535161 CAPLUS
DN 77:135161
TI Antitumor alkaloids from Cephalotaxus harringtonia. Structure and activity
AU Powell, R. G.; Weisleder, D.; Smith, C. R., Jr.
CS North. Reg. Res. Lab., Agric. Res. Serv., Peoria, Ill., USA
SO J. Pharm. Sci. (1972), 61(8), 1227-30
CODEN: JPMSAE
DT Journal
LA English
CC 1-5 (Pharmacodynamics)
AB Cephalotaxine (I) [24316-19-6] and a no. of its esters were isolated from the plant C. harringtonia and tested for antitumor activity. I was inactive, but harringtonine (II) [**26833-85-2**], isoharringtonine (III) [26833-86-3], homoharringtonine (IV) [26833-87-4], and deoxyharringtonine (V) [36804-95-2] had antitumor activity against exptl. P388 and L1210 leukemia in mice.
ST cephalotaxine antitumor action; harringtonine leukemia; **cancer** cephalotaxine
IT Cephalotaxus harringtonia
(alkaloids of, neoplasm inhibition by)
IT Neoplasm inhibitors
(cephalotaxine esters)
IT Nuclear magnetic resonance
(of cephalotaxine esters)
IT 24274-60-0
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(neoplasm inhibiting activity of)
IT 24316-19-6
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibiting activity of, ester derivs. in relation to)
IT **26833-85-2** 26833-86-3 26833-87-4 36804-95-2
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by)
IT 38535-03-4P 38535-04-5P 38535-05-6P 38535-06-7P 38535-07-8P
38535-08-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

=>

---Logging off of STN---

=>
Executing the logoff script...

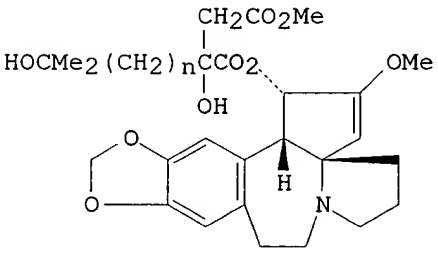
=> LOG Y

COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST	40.89	47.26
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.29	-9.29

STN INTERNATIONAL LOGOFF AT 10:26:47 ON 31 JAN 2002

AN 1983:27435 CAPLUS
DN 98:27435
TI Antitumor activities of harringtonine and homoharringtonine, Cephalotaxus alkaloids which are active principles from plant by intraperitoneal and oral administration
AU Takeda, Setsuo; Yajima, Nobuhiro; Kitazato, Kenji; Unemi, Norio
CS Res. Inst., Taiho Pharm. Co., Ltd., Kawauchi, 771-01, Japan
SO J. Pharmacobio-Dyn. (1982), 5(10), 841-7
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
CC 1-6 (Pharmacology)
GI

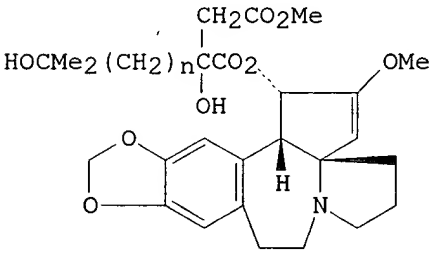


I, n=2
II, n=3

AB The antitumor activities of the Cephalotaxus alkaloids harringtonine (HA)(I) [26833-85-2] and homoharringtonine (HO)(II) [**26833-87-4**], were compared with those of the Vinca alkaloids vincristine (VCR) and vinblastine (VLB). HA and HO had significant activities against P388 **leukemia**, L1210 **leukemia**, and B16 melanoma by i.p. **injection** comparable to VCR and VLB. The therapeutic indexes (LD10/ED50) of HA and HO in B16 melanoma system were 1.90 and 2.31, while those of VCR and VLB were 1.38 and <1.00, resp. The oral administration of the Cephalotaxus alkaloids evoked a significant antitumor activity; Vinca alkaloids, however, induced no activity against P388 and B16 melanoma. The efficacy of HO on various tumor systems was equal or greater than that of HA. In contrast to VCR and VLB, HA and HO demonstrated moderate activity against P388/VCR, a subline of P388 resistant to vincristine. The i.p. **injection** of VCR or VLB produced an increase in the mitotic index of P388 cells as compared with the control values, but HA or HO decreased it. Apparently, HA and HO are a new class of active compds. of plant origin which may differ from the vinca alkaloids in the mechanism of antitumor activity.
ST Cephalotaxus alkaloid antitumor; antitumor harringtonine homoharringtonine
IT Cephalotaxus
(alkaloids from, neoplasm-inhibiting activity of)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from Cephalotaxus, neoplasm-inhibiting activity of)
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of)

AN 1983:172715 CAPLUS
DN 98:172715
TI Ultrastructural and electron-microscope autoradiographic study on the mechanism of therapeutic effect of semisynthetic harringtonine and homoharringtonine on L1210 leukemic mouse cells
AU Li, Kun; Chao, Weimin; Han, Rui; Pan, Zhenkun
CS Inst. Basic Med., Acad. Med. Sci., Peop. Rep. China
SO Zhonghua Yixue Zazhi (1983), 63(1), 29-32
CODEN: CHHTAT; ISSN: 0300-2578
DT Journal
LA Chinese
CC 1-6 (Pharmacology)
GI



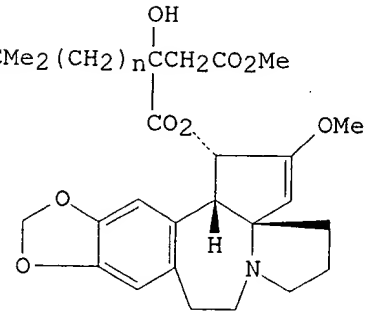
I, n=2
II, n=3

AB **Injection** (i.p.) of harringtonine (I) [26833-85-2] (26 mg/kg) and homoharringtonine (II) [**26833-87-4**] (1 mg/kg) into L1210 leukemic mice both produced apoptosis (Searle, J., et al., 1975) in leukemic cells. There were fewer or no Ag grains from [3H]thymidine deposition in the nuclei of the leukemic cells either with or without ultrastructural changes after I or II treatment, indicating that DNA synthesis is severely inhibited. II often caused swelling of the nuclear membrane, endoplasmic reticulum, Golgi app., and mitochondria as well as expansion of perinuclear space, formation of membrane vacuoles in the nuclei, and appearance of 1 type of small membrane-bound organelle which has not been reported before. II was found to have stronger effects on L1210 leukemic cells than I.
ST **leukemia** inhibition harringtonine homoharringtonine
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as, cell morphol. in relation to)

IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, cell morphol. in relation to)

AN 1981:234 CAPLUS
DN 94:234
TI Pharmacology of harringtonine and homoharringtonine
AU Chen, Sui-Ting; Hua, Che; Hsi, Shen
CS Shanghai Inst. Pharmcol., Acad. Sin., Shanghai, Peop. R. China
SO K'o Hsueh T'ung Pao (1980), 25(18), 859-61
CODEN: KHTPAT; ISSN: 0023-074X
DT Journal
LA Chinese
CC 1-5 (Pharmacodynamics)

GI



I, n=2
II, n=3

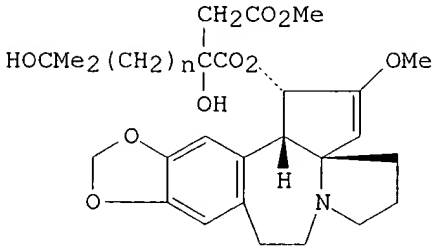
AB I.p. **injection** of harringtonine (I) [26833-85-2] and homoharringtonine (II) [**26833-87-4**] (1-1.5 mg/kg) inhibited the growth of brain tumor and **leukemia** (L615) in rats by 42 and 40%, resp., and increased survival by 124 and 32%, resp. However, both I and II were ineffective against Ehrlich ascites tumor and sarcoma. The radioactivity of I-3H and II-3H injected i.p. appeared in the blood and various organs examd., including the brain and bone within 1 h; however, the activities were always greater in the liver and kidney than other organs studied. The appearance of I-3H in various organs and urine and feces was greater than that of II-3H; 27.6 and 16.0%, resp. of the i.p. injected I-3H and II-3H appeared in the urine, and the corresponding appearance of I-3H and II-3H in the feces was 11.2% and 3.6%, resp. The half-life of I and II in the blood was 13 and 32 min, resp.

ST harringtonine homoharringtonine antitumor pharmacokinetics

IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: PROC (Process)
(neoplasm inhibiting activity and pharmacokinetics of)

AN 1983:27435 CAPLUS
DN 98:27435
TI Antitumor activities of harringtonine and homoharringtonine, Cephalotaxus alkaloids which are active principles from plant by intraperitoneal and oral administration
AU Takeda, Setsuo; Yajima, Nobuhiro; Kitazato, Kenji; Unemi, Norio
CS Res. Inst., Taiho Pharm. Co., Ltd., Kawauchi, 771-01, Japan
SO J. Pharmacobio-Dyn. (1982), 5(10), 841-7
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
CC 1-6 (Pharmacology)
GI

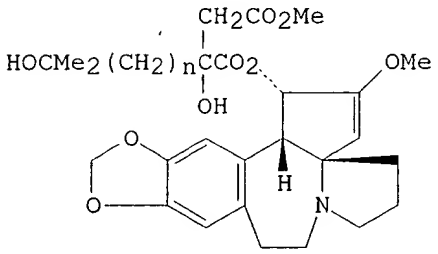


I, n=2
II, n=3

AB The antitumor activities of the Cephalotaxus alkaloids harringtonine (HA)(I) [26833-85-2] and homoharringtonine (HO)(II) [**26833-87-4**], were compared with those of the Vinca alkaloids vincristine (VCR) and vinblastine (VLB). HA and HO had significant activities against P388 **leukemia**, L1210 **leukemia**, and B16 melanoma by i.p. **injection** comparable to VCR and VLB. The therapeutic indexes (LD10/ED50) of HA and HO in B16 melanoma system were 1.90 and 2.31, while those of VCR and VLB were 1.38 and <1.00, resp. The oral administration of the Cephalotaxus alkaloids evoked a significant antitumor activity; Vinca alkaloids, however, induced no activity against P388 and B16 melanoma. The efficacy of HO on various tumor systems was equal or greater than that of HA. In contrast to VCR and VLB, HA and HO demonstrated moderate activity against P388/VCR, a subline of P388 resistant to vincristine. The i.p. **injection** of VCR or VLB produced an increase in the mitotic index of P388 cells as compared with the control values, but HA or HO decreased it. Apparently, HA and HO are a new class of active compds. of plant origin which may differ from the vinca alkaloids in the mechanism of antitumor activity.
ST Cephalotaxus alkaloid antitumor; antitumor harringtonine homoharringtonine
IT Cephalotaxus
(alkaloids from, neoplasm-inhibiting activity of)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from Cephalotaxus, neoplasm-inhibiting activity of)
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of)

AN 1983:172715 CAPLUS
DN 98:172715
TI Ultrastructural and electron-microscope autoradiographic study on the mechanism of therapeutic effect of semisynthetic harringtonine and homoharringtonine on L1210 leukemic mouse cells
AU Li, Kun; Chao, Weimin; Han, Rui; Pan, Zhenkun
CS Inst. Basic Med., Acad. Med. Sci., Peop. Rep. China
SO Zhonghua Yixue Zazhi (1983), 63(1), 29-32.
CODEN: CHHTAT; ISSN: 0300-2578
DT Journal
LA Chinese
CC 1-6 (Pharmacology)
GI



I, n=2
II, n=3

AB **Injection** (i.p.) of harringtonine (I) [26833-85-2] (26 mg/kg) and homoharringtonine (II) [**26833-87-4**] (1 mg/kg) into L1210 leukemic mice both produced apoptosis (Searle, J., et al., 1975) in leukemic cells. There were fewer or no Ag grains from [3H]thymidine deposition in the nuclei of the leukemic cells either with or without ultrastructural changes after I or II treatment, indicating that DNA synthesis is severely inhibited. II often caused swelling of the nuclear membrane, endoplasmic reticulum, Golgi app., and mitochondria as well as expansion of perinuclear space, formation of membrane vacuoles in the nuclei, and appearance of 1 type of small membrane-bound organelle which has not been reported before. II was found to have stronger effects on L1210 leukemic cells than I.
ST **leukemia** inhibition harringtonine homoharringtonine
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as, cell morphol. in relation to)

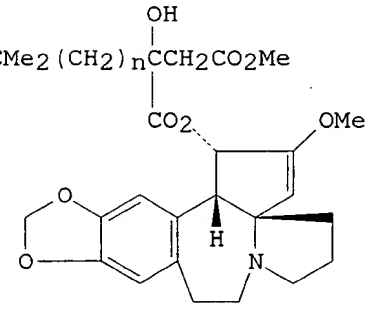
IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, cell morphol. in relation to)

AN 2000:47497 CAPLUS
DN 132:73342
TI A phase II trial of homoharringtonine and caracemide in the treatment of patients with advanced large bowel **cancer**
AU Witte, Robert S.; Lipsitz, Stuart; Goodman, Thomas L.; Asbury, Robert F.; Wilding, George; Strnad, Charles M.; Smith, Thomas J.; Haller, Daniel G.
CS Gundersen Lutheran, La Crosse, WI, USA
SO Invest. New Drugs (1999), 17(2), 173-177
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Twenty-four previously untreated, ambulatory patients with advanced colorectal carcinoma were treated with either caracemide (11 patients) or homoharringtonine (13 patients). No objective responses were obsd. in any of the treatment cohorts. Caracemide was well tolerated with the exception of one death due to sepsis. On the homoharringtonine arm one patient died of pulmonary sepsis, one patient experienced grade 4 leukopenia requiring more than 4 wk of recovery, and an addnl. patient developed grade 4 renal failure. These severe and unexpected complications caused early termination of accrual to the homoharringtonine arm of the study. These agents have no activity in the treatment of advanced colorectal carcinoma.
ST homoharringtonine caracemide colorectal carcinoma antitumor
IT Intestine, neoplasm
(colorectal carcinoma, inhibitors; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT Antitumor agents
(colorectal carcinoma; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT **26833-87-4**, Homoharringtonine 81424-67-1, Caracemide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)

AN 2000:47497 CAPLUS
DN 132:73342
TI A phase II trial of homoharringtonine and caracemide in the treatment of patients with advanced large bowel **cancer**
AU Witte, Robert S.; Lipsitz, Stuart; Goodman, Thomas L.; Asbury, Robert F.; Wilding, George; Strnad, Charles M.; Smith, Thomas J.; Haller, Daniel G.
CS Gundersen Lutheran, La Crosse, WI, USA
SO Invest. New Drugs (1999), 17(2), 173-177
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Twenty-four previously untreated, ambulatory patients with advanced colorectal carcinoma were treated with either caracemide (11 patients) or homoharringtonine (13 patients). No objective responses were obsd. in any of the treatment cohorts. Caracemide was well tolerated with the exception of one death due to sepsis. On the homoharringtonine arm one patient died of pulmonary sepsis, one patient experienced grade 4 leukopenia requiring more than 4 wk of recovery, and an addnl. patient developed grade 4 renal failure. These severe and unexpected complications caused early termination of accrual to the homoharringtonine arm of the study. These agents have no activity in the treatment of advanced colorectal carcinoma.
ST homoharringtonine caracemide colorectal carcinoma antitumor
IT Intestine, neoplasm
(colorectal carcinoma, inhibitors; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT Antitumor agents
(colorectal carcinoma; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT **26833-87-4**, Homoharringtonine 81424-67-1, Caracemide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)

AN 1981:234 CAPLUS
DN 94:234
TI Pharmacology of harringtonine and homoharringtonine
AU Chen, Sui-Ting; Hua, Che; Hsi, Shen
CS Shanghai Inst. Pharmcol., Acad. Sin., Shanghai, Peop. R. China
SO K'o Hsueh T'ung Pao (1980), 25(18), 859-61
CODEN: KHTPAT; ISSN: 0023-074X
DT Journal
LA Chinese
CC 1-5 (Pharmacodynamics)

GI



I, n=2
II, n=3

AB I.p. **injection** of harringtonine (I) [26833-85-2] and homoharringtonine (II) [**26833-87-4**] (1-1.5 mg/kg) inhibited the growth of brain tumor and **leukemia** (L615) in rats by 42 and 40%, resp., and increased survival by 124 and 32%, resp. However, both I and II were ineffective against Ehrlich ascites tumor and sarcoma. The radioactivity of I-3H and II-3H injected i.p. appeared in the blood and various organs examd., including the brain and bone within 1 h; however, the activities were always greater in the liver and kidney than other organs studied. The appearance of I-3H in various organs and urine and feces was greater than that of II-3H; 27.6 and 16.0%, resp. of the i.p. injected I-3H and II-3H appeared in the urine, and the corresponding appearance of I-3H and II-3H in the feces was 11.2% and 3.6%, resp. The half-life of I and II in the blood was 13 and 32 min, resp.

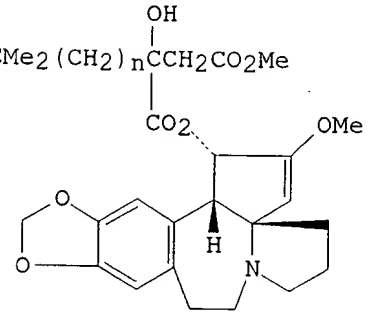
ST harringtonine homoharringtonine antitumor pharmacokinetics

IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: PROC (Process)
(neoplasm inhibiting activity and pharmacokinetics of)

AN 1981:234 CAPLUS
DN 94:234
TI Pharmacology of har gtonine and homoharringtonine
AU Chen, Sui-Ting; Hua, Che; Hsi, Shen
CS Shanghai Inst. Pharmcol., Acad. Sin., Shanghai, Peop. R. China
SO K'o Hsueh T'ung Pao (1980), 25(18), 859-61
CODEN: KHTPAT; ISSN: 0023-074X
DT Journal
LA Chinese
CC 1-5 (Pharmacodynamics)

GI



I, n=2
II, n=3

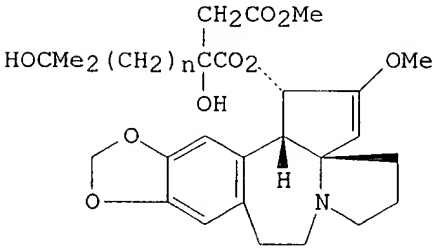
AB I.p. **injection** of harringtonine (I) [26833-85-2] and homoharringtonine (II) [**26833-87-4**] (1-1.5 mg/kg) inhibited the growth of brain tumor and **leukemia** (L615) in rats by 42 and 40%, resp., and increased survival by 124 and 32%, resp. However, both I and II were ineffective against Ehrlich ascites tumor and sarcoma. The radioactivity of I-3H and II-3H injected i.p. appeared in the blood and various organs examd., including the brain and bone within 1 h; however, the activities were always greater in the liver and kidney than other organs studied. The appearance of I-3H in various organs and urine and feces was greater than that of II-3H; 27.6 and 16.0%, resp. of the i.p. injected I-3H and II-3H appeared in the urine, and the corresponding appearance of I-3H and II-3H in the feces was 11.2% and 3.6%, resp. The half-life of I and II in the blood was 13 and 32 min, resp.

ST harringtonine homoharringtonine antitumor pharmacokinetics

IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: PROC (Process)
(neoplasm inhibiting activity and pharmacokinetics of)

AN 1983:27435 CAPLUS
DN 98:27435
TI Antitumor activities of harringtonine and homoharringtonine, Cephalotaxus alkaloids which are active principles from plant by intraperitoneal and oral administration
AU Takeda, Setsuo; Yajima, Nobuhiro; Kitazato, Kenji; Unemi, Norio
CS Res. Inst., Taiho Pharm. Co., Ltd., Kawauchi, 771-01, Japan
SO J. Pharmacobio-Dyn. (1982), 5(10), 841-7
CODEN: JOPHDQ; ISSN: 0386-846X
DT Journal
LA English
CC 1-6 (Pharmacology)
GI

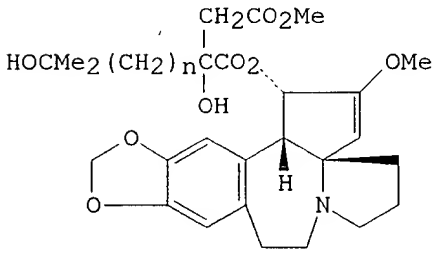


I, n=2
II, n=3

AB The antitumor activities of the Cephalotaxus alkaloids harringtonine (HA)(I) [26833-85-2] and homoharringtonine (HO)(II) [**26833-87-4**], were compared with those of the Vinca alkaloids vincristine (VCR) and vinblastine (VLB). HA and HO had significant activities against P388 **leukemia**, L1210 **leukemia**, and B16 melanoma by i.p. **injection** comparable to VCR and VLB. The therapeutic indexes (LD10/ED50) of HA and HO in B16 melanoma system were 1.90 and 2.31, while those of VCR and VLB were 1.38 and <1.00, resp. The oral administration of the Cephalotaxus alkaloids evoked a significant antitumor activity; Vinca alkaloids, however, induced no activity against P388 and B16 melanoma. The efficacy of HO on various tumor systems was equal or greater than that of HA. In contrast to VCR and VLB, HA and HO demonstrated moderate activity against P388/VCR, a subline of P388 resistant to vincristine. The i.p. **injection** of VCR or VLB produced an increase in the mitotic index of P388 cells as compared with the control values, but HA or HO decreased it. Apparently, HA and HO are a new class of active compds. of plant origin which may differ from the vinca alkaloids in the mechanism of antitumor activity.
ST Cephalotaxus alkaloid antitumor; antitumor harringtonine homoharringtonine
IT Cephalotaxus
(alkaloids from, neoplasm-inhibiting activity of)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from Cephalotaxus, neoplasm-inhibiting activity of)
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as)

IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of)

AN 1983:172715 CAPLUS
DN 98:172715
TI Ultrastructural and electron-microscope autoradiographic study on the mechanism of therapeutic effect of semisynthetic harringtonine and homoharringtonine on L1210 leukemic mouse cells
AU Li, Kun; Chao, Weimin; Han, Rui; Pan, Zhenkun
CS Inst. Basic Med., Acad. Med. Sci., Peop. Rep. China
SO Zhonghua Yixue Zazhi (1983), 63(1), 29-32.
CODEN: CHHTAT; ISSN: 0300-2578
DT Journal
LA Chinese
CC 1-6 (Pharmacology)
GI



I, n=2
II, n=3

AB **Injection** (i.p.) of harringtonine (I) [26833-85-2] (26 mg/kg) and homoharringtonine (II) [**26833-87-4**] (1 mg/kg) into L1210 leukemic mice both produced apoptosis (Searle, J., et al., 1975) in leukemic cells. There were fewer or no Ag grains from [3H]thymidine deposition in the nuclei of the leukemic cells either with or without ultrastructural changes after I or II treatment, indicating that DNA synthesis is severely inhibited. II often caused swelling of the nuclear membrane, endoplasmic reticulum, Golgi app., and mitochondria as well as expansion of perinuclear space, formation of membrane vacuoles in the nuclei, and appearance of 1 type of small membrane-bound organelle which has not been reported before. II was found to have stronger effects on L1210 leukemic cells than I.
ST **leukemia** inhibition harringtonine homoharringtonine
IT Neoplasm inhibitors
(harringtonine and homoharringtonine as, cell morphol. in relation to)

IT 26833-85-2 **26833-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, cell morphol. in relation to)

AN 2000:47497 CAPLUS
DN 132:73342
TI A phase II trial of homoharringtonine and caracemide in the treatment of patients with advanced large bowel **cancer**
AU Witte, Robert S.; Lipsitz, Stuart; Goodman, Thomas L.; Asbury, Robert F.; Wilding, George; Strnad, Charles M.; Smith, Thomas J.; Haller, Daniel G.
CS Gundersen Lutheran, La Crosse, WI, USA
SO Invest. New Drugs (1999), 17(2), 173-177
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Twenty-four previously untreated, ambulatory patients with advanced colorectal carcinoma were treated with either caracemide (11 patients) or homoharringtonine (13 patients). No objective responses were obsd. in any of the treatment cohorts. Caracemide was well tolerated with the exception of one death due to sepsis. On the homoharringtonine arm one patient died of pulmonary sepsis, one patient experienced grade 4 leukopenia requiring more than 4 wk of recovery, and an addnl. patient developed grade 4 renal failure. These severe and unexpected complications caused early termination of accrual to the homoharringtonine arm of the study. These agents have no activity in the treatment of advanced colorectal carcinoma.
ST homoharringtonine caracemide colorectal carcinoma antitumor
IT Intestine, neoplasm
(colorectal carcinoma, inhibitors; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT Antitumor agents
(colorectal carcinoma; toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)
IT **26833-87-4**, Homoharringtonine 81424-67-1, Caracemide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity and efficacy of homoharringtonine and caracemide in treatment of humans with advanced large bowel **cancer**)